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09/701,623	12/01/2000	Chang Yi Wang	1151-4153US1	8939

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EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	22

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,623	WANG ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-29* is/are pending in the application.

4a) Of the above claim(s) *3-18 and 21-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 19-20 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 2-29 are pending.

2. Claims 3-18 and 21-28 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. The request for modification of the restriction requirement to include claims 3-18, and 20-25 in the present application is acknowledged. However, the inventions listed as Groups 1-60 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the same reasons as set forth in the restriction mailed 3/20/02. Further, a cyclized peptide (claims 29, 2, 19, and 20) drawn to class 514 and subclass 11 whereas claims 3-18 and 21-28 are drawn to linear peptide comprises helper T epitope and IgE-CH3 domain, drawn to Class 530, subclass 300. A search of one will not encompass the other. It is a burden to search more than one invention. Therefore, the requirement of Group 1 (now claims 29, 2, 19 and 20) and Groups 2-60 is still deemed proper and is therefore made FINAL.

4. The following new grounds of rejection are necessitated by the amendment filed 1/10/03.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 19-20 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) an IgE-CH3 domain antigen peptide useful for eliciting antibodies that inhibit the binding of IgE to basophils and mast cells said peptide consisting of an amino acid sequence from about 25 to about 29 amino acids in length cyclized with two terminal cysteine residues separated by about 23 amino acids residues, the sequence of said peptide corresponds to amino acid 413-435 of the epsilon heavy chain human IgE-CH3 domain, (2) an IgE-CH3 domain peptide selected from the group consisting of SEQ ID NO: 5-8 and 84 for treating eliciting antibodies that inhibit the binding of IgE to basophils and mast cells, (3) A

peptide conjugate comprising a carrier protein covalently attached to one or more IgE-CH3 domain antigen peptide useful for eliciting antibodies that inhibit the binding of IgE to basophils and mast cells said peptide consisting of an amino acid sequence from about 25 to about 29 amino acids in length cyclized with two terminal cysteine residues separated by about 23 amino acids residues, the sequence of said peptide corresponds to amino acid 413-435 of the epsilon heavy chain human IgE-CH3 domain, and (4) the said peptide conjugate wherein the carrier protein is keyhole limpet hemocyanin, **does not** reasonably provide enablement for (1) *any* IgE-CH3 domain antigen peptide, (2) *any* analog as set forth in claims 29, and (3) *any* peptide conjugate as set forth in claims 19-20 for eliciting antibodies that inhibit the binding of IgE to basophils and mast cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only four full length IgE polypeptide from human (SEQ ID NO: 1), dog (SEQ ID NO: 2), rat (SEQ ID NO: 3), and mouse (SEQ ID NO: 4). The specification further discloses various modified IgE CH3 domain antigen peptides from human such as the ones disclosed in Table 2 either having a native Cysteine at position 358 or 312 or 418 of SEQ ID NO: 1 conservatively substitute with a serine (SEQ ID NO: 28-35) or having a cysteine residue inserted at the N and the C terminal of CH2, CH3 or CH4 domain. The peptides mentioned above are covalently crosslinked with a carrier molecule such as KLH by conventional glutaraldehyde or MBS (m-Maleimidobenzoyl-N-hydroxysuccinimide ester or helper T epitope such as SEQ ID NO: 10-13, and the ones shown in Tables 5 and 6 where CH3 domains are crosslinked to Th helper epitope or Invasin domain. The specification discloses cyclic peptide. The peptides shown in Table 2 are screened for cross-reactivity with human IgE (Table 2 on pages 69-73) and inhibition of histamine release (Table 3 on page 74). The specification further

discloses that only anti-IgE antibodies generated from peptide of SEQ ID NO: 5 crossed linked to the specific synthetic Th epitope (Th (1,2,4)- or invasin-GG-Synthetic T helper epitope (1,2,4)-GG- (Table 5) significantly inhibit Histamine release while anti-IgE antibody generated from other peptides such as SEQ ID NO: 28-38 crosslinked to KLH or crosslinked to Th epitope such as SEQ ID NO: 46, 55 and 57 do not inhibit histamine release (Table 3).

The specification does not teach how to make and use *any* IgE-CH3 domain antigen peptide wherein the sequence of said peptide corresponds to amino acid 413 to 435 of the heavy chain of any mammalian IgE-CH3, any analogue of said IgE-CH3 domain antigen peptide wherein from one to four of any residues in amino acid 413 to 435 of any mammalian IgE-CH3 peptide are conservatively substituted, inserted or deleted because of the following reasons. First, the term "is" is open-ended. It expands the peptide to include additional amino acid at either or both ends. There is no guidance as to which amino acids to be added and whether the peptide would elicit antibodies that binds specifically to *any* IgE-CH3 domain, in turn, the antibodies inhibit the binding of IgE to basophils and mast cells. Second, the "AA413-AA435" of the epsilon heavy chain of which mammalian IgE-CH3 is not clear because the specific SEQ ID NO is not recited in the claim. Without the SEQ ID NO, there is no structure to the sequence, let alone which amino acid such as "AA413-AA435" is referred to which sequence. The specification discloses on page 26 that AA413-AA435 is referring to the human IgE-CH3 of SEQ ID NO: 1, and not any mammalian IgE-CH3. Further, it is noted that the heavy chain of IgE from mouse, rat, dog and human are different length (Table 1). The amino acid 413-435 in human may be different from that of mouse, rat, dog and cat. Third, with regard to peptide analog, even if the IgE-CH3 domain antigen peptide is limited to human, mouse, rat and dog, there is no guidance as to which one to four amino acid residues within the epsilon heavy chain of IgE-CH3 domain can be conservatively substituted, much less inserted or deleted and whether the resulting IgE-CH3 peptide would eliciting antibodies that bind specifically to the IgE-CH3, in turn, would inhibit the binding of IgE to basophils and mast cells.

Ngo *et al*, of record, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Kuby *et al* teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific

conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide.

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the indefinite number of undisclosed IgE-CH3 domain antigen peptide, it is unpredictable which undisclosed "IgE-CH3 domain antigen peptide would be effective for eliciting antibodies that inhibit the binding of IgE to basophils and mast cells for treating allergy. Since the antigen-peptide and analog are not enabled, it follows that any peptide conjugate comprising any carrier protein covalently attached to one or more of any non-enabling IgE-CH3 domain antigen peptide is not enabled.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 1/10/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) the claimed peptide corresponds with a specific segment of the IgE and has been shown to be effective for eliciting antibodies that are effective in inhibiting the binding of IgE to basophils and mast cells. Although the sequence may vary, a person with skill in the art would be able to identify AA413-AA435 of IgE. It merely requires alignment of the specific IgE sequence with that published for human IgE and count to AA413 to AA435. (2) the present claim 29 and claims dependent thereon are directed to a short peptide of 23 amino acids which cyclized by the terminal cysteines. Applicants have shown that substitutions of cysteines with serine did not affect the immunogenicity of the claimed peptide.

However, the "AA413 to AA435" in reference to which IgE sequence is not clear. The claims encompass any mammalian IgE-CH3 domain antigen peptide and any analogue. Further,

the term "is" is open-ended. It expands the peptide to include additional amino acid at either or both ends. There is no guidance as to which amino acids to be added and whether the peptide would elicit antibodies that binds specifically to *any* IgE-CH3 domain, in turn, the antibodies inhibit the binding of IgE to basophils and mast cells. Second, the "AA413-AA435" of the epsilon heavy chain of which mammalian IgE-CH3 is not clear because the specific SEQ ID NO is not recited in the claim. Without the SEQ ID NO, it is not clear the amino acid such as "AA413-AA435" are in reference to which mammalian IgE CH3 domain sequence. The specification discloses on page 26 that AA413-AA435 is referring to the human IgE-CH3 of SEQ ID NO: 1, and not any just any mammalian IgE-CH3. Further, it is noted that the heavy chain of IgE from mouse, rat, dog and human are different length (Table 1). The amino acid 413-435 in human may be different from that of mouse, rat, dog and cat. Third, with regard to peptide analog, even if the IgE-CH3 domain antigen peptide is limited to human, mouse, rat and dog, there is no guidance as to which one to four amino acid residues within the epsilon heavy chain of IgE-CH3 domain can be conservatively substituted, much less inserted or deleted and whether the resulting IgE-CH3 peptide would eliciting antibodies that bind specifically to the IgE-CH3 domain, in turn, would inhibit the binding of IgE to basophils and mast cells.

Ngo *et al*, of record, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Kuby *et al* teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide.

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the indefinite number of undisclosed IgE-CH3 domain antigen peptide, it is unpredictable which undisclosed "IgE-CH3 domain antigen peptide would be effective for eliciting antibodies that inhibit the binding of IgE to basophils and mast cells for treating allergy. Since the antigen-peptide and analog are not enabled, it follows that any peptide

conjugate comprising any carrier protein covalently attached to one or more of any non-enabling IgE-CH3 domain antigen peptide is not enabled.

7. Claims 19-20 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* IgE-CH3 domain antigen peptide, (2) *any* analog as set forth in claims 29, and (3) *any* peptide conjugate as set forth in claims 19-20 for eliciting antibodies that inhibit the binding of IgE to basophils and mast cells.

The specification discloses only the full length IgE polypeptide from human (SEQ ID NO: 1), dog (SEQ ID NO: 2), rat (SEQ ID NO: 3), and mouse (SEQ ID NO: 4). The specification further discloses various modified IgE CH3 domain antigen peptides from human such as the ones disclosed in Table 2 either having a native Cysteine at position 358 or 312 or 418 of SEQ ID NO: 1 conservatively substitute with a serine (SEQ ID NO: 28-35) or having a cysteine residue inserted at the N and the C terminal of CH2, CH3 or CH4 domain. The peptides mentioned above are covalently crosslinked with a carrier molecule such as KLH by conventional glutaraldehyde or MBS (m-Maleimidobenzoyl-N-hydroxysuccinimide ester or helper T epitope such as SEQ ID NO: 10-13, and the ones shown in Tables 5 and 6 where CH3 domains are crosslinked to Th helper epitope or Invasin domain. The specification discloses cyclic peptide. The peptides shown in Table 2 are screened for cross-reactivity with human IgE (Table 2 on pages 69-73) and inhibition of histamine release (Table 3 on page 74). The specification further discloses that only anti-IgE antibodies generated from peptide of SEQ ID NO: 5 crossed linked to the specific synthetic Th epitope (Th (1,2,4)- or invasin-GG-Synthetic T helper epitope (1,2,4)-GG- (Table 5) significantly inhibit Histamine release while anti-IgE antibody generated from other peptides such as SEQ ID NO: 28-38 crosslinked to KLH or crosslinked to Th epitope such as SEQ ID NO: 46, 55 and 57 do not inhibit histamine release (Table 3).

With the exception of the specific peptides mentioned above, there is insufficient written description about the structure associated with function of *any* IgE-CH3 domain antigen peptide because the term "is" is open-ended. It expands the peptide to include additional amino acids at either or both ends. There is inadequate written description about which amino acids to be added

and whether the peptide would elicit antibodies that binds specifically to *any* IgE-CH3 domain, in turn, the antibodies inhibit the binding of IgE to basophils and mast cells. Second, it is not clear the "AA413-AA435" of the epsilon heavy chain is reference to which mammalian IgE-CH3 since the specific SEQ ID NO is not recited in the claim. Without the SEQ ID NO, there is no structure to the sequence, let alone which amino acid such as "AA413-AA435" is referred to which sequence. The specification discloses on page 26 that AA413-AA435 is referring to the human IgE-CH3 of SEQ ID NO: 1, and not any mammalian IgE-CH3. Further, it is noted that the heavy chain of IgE from mouse, rat, dog and human are different length (Table 1). The amino acid 413-435 in human may be different from that of mouse, rat, dog and cat. Third, with regard to peptide analog, even if the IgE-CH3 domain antigen peptide is limited to human, mouse, rat and dog, there is inadequate written description about the structure, much less about the function of any undisclosed analog. There is inadequate written description about which one to four amino acid residues within the epsilon heavy chain of IgE-CH3 domain can be conservatively substituted, inserted or deleted and whether the resulting IgE-CH3 domain antigen peptide analog would eliciting antibodies that bind specifically to the IgE-CH3, in turn, would inhibit the binding of IgE to basophils and mast cells. Since the antigen-peptide and analog are not adequately describe, it follows that any peptide conjugate comprising any carrier protein covalently attached to one or more of any non-enabling IgE-CH3 domain antigen peptide are not adequately described. Further, applicant discloses only five IgE-CH3 domain from human, mouse, rat, dog and horse. Given the lack of any additional representative species of IgE-CH3 domain antigen peptide and analog from other species, the peptide sequence corresponds to AA413-AA435 of the epsilon heavy chain of any mammalian IgE-CH3 is not adequately described. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant's arguments filed 1/10/03 have been fully considered but are not found persuasive.

Applicant's position is that (1) Claim 29 is directed to AA413-AA435 of mammalian IgE circularized by modification of the terminal ends of the peptide with cysteines. The specification clearly describes a peptide that corresponds to AA413-AA435 of various mammalian IgE,

including that of human IgE, dog IgE, mice IgE, rat IgE, and horse IgE (page 36, lines 27 to page 37, line 2). (2) Applicant had describe analogs with substitutions, and additions. (3) the Examiner cites University of California v. Eli Lilly for the proposition that Applicants are not in possession of the claimed homologs and analogs. This case is directed to a claim for human DNA for insulin. The present case is not about DNA.

In response, it is not clear that the "AA413-AA435" of the epsilon heavy chain is in reference to which mammalian IgE-CH3 since the specific SEQ ID NO is not recited in the claim. Without the SEQ ID NO, there is no structure to the sequence, let alone which amino acid such as "AA413-AA435" is referred to which sequence. The specification discloses on page 26 that AA413-AA435 is referring to the human IgE-CH3 of SEQ ID NO: 1, and not any mammalian IgE-CH3. Further, it is noted that the heavy chain of IgE from mouse, rat, dog and human are different length (Table 1). The amino acid 413-435 in human may be different from that of mouse, rat, dog and cat. Third, with regard to peptide analog, even if the IgE-CH3 domain antigen peptide is limited to human, mouse, rat and dog, there is inadequate written description about the structure, much less about the function of any undisclosed analog. There is inadequate written description about which one to four amino acid residues within the epsilon heavy chain of IgE-CH3 domain can be conservatively substituted, inserted or deleted and whether the resulting IgE-CH3 domain antigen peptide analog would eliciting antibodies that bind specifically to the IgE-CH3, in turn, would inhibit the binding of IgE to basophils and mast cells. Since the antigen-peptide and analog are not adequately describe, it follows that any peptide conjugate comprising any carrier protein covalently attached to one or more of any non-enabling IgE-CH3 domain antigen peptide are not adequately described. Further, applicant discloses only five IgE-CH3 domain from human, mouse, rat, dog and horse. Given the lack of any additional representative species of IgE-CH3 domain antigen peptide and analog from other species, the peptide sequence corresponds to AA413-AA435 of the epsilon heavy chain of any mammalian IgE-CH3 is not adequately described. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 2, 19-20 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of " AA413-AA435 of the epsilon heavy chain of a mammalian IgE-CH3" in claim 29 is ambiguous and indefinite because it is not clear that the "AA413-AA435" of the epsilon heavy chain is in reference to which mammalian IgE-CH3 since the specific SEQ ID NO is not recited in the claim. The specification discloses on page 26 that AA413-AA435 is referring to the human IgE-CH3 of SEQ ID NO: 1, and not just any mammalian IgE-CH3.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

11. The filing date of the instant claims 29, 2, 19 and 20 are deemed to be the filing date of the PCT/US99/13959 filed 6/21/99, as the parent application is drawn only to novel peptide for eliciting antibodies to LHRH comprising T helper cell epitope covalently linked to LHRH, and thus does not support the claimed limitations of an IgE-CH3 domain antigen peptide useful for eliciting antibodies that inhibit the binding of IgE to basophils and mast cells said peptide is about 25 and about 29 amino acids in length cyclized with two cysteine residues separated by about 23 amino acid residues, the sequence of said peptide corresponds to AA413 to A435 of the epsilon heavy chain of a mammalian IgE-CH3 and an analogue of the peptide wherein from one to four of the residues in AA413-AA435 are conservatively substituted, inserted, or deleted of the instant application.

12. Claims 2, 19-20 and 29 are rejected under 35 U.S.C. 102(e) (2) as being anticipated by US Pat No. 6,025,468 A (Feb 2000, PTO 892).

The '468 patent teaches an antigen peptide such as SEQ ID NO: 95 that is 25 amino acid in length, which is about 25 and about 29 amino acids in length and the reference peptide containing two terminal cysteine residues separated by 23 amino acid residues that is capable of cyclized between said two cysteine residues by forming disulfide bond (See SEQ ID NO: 95 of '468 patent, in particular). The reference peptide is 100% identical to the claimed peptide of SEQ ID NO: 5. The reference peptide inherently is useful for eliciting antibodies that inhibiting the binding of IgE to basophils and mast cells since it is an IgE-CH3 domain from a mammal such as human. The '468 patent further teaches that the reference peptide is conjugated or covalently linked to a carrier such as keyhole limpet hemocyanin (KLH) (See column 16, line 34, in particular). Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 1/10/03 have been fully considered but are not found persuasive.

Applicants' position is that the present application enjoys an effective filing date of June 20, 1998. The parent application serial no. 09/100,287 was filed on the same day, June 20, 1998.

However, the parent application 09/100,287 does not have support for the claimed limitation of an IgE-CH3 domain antigen peptide useful for eliciting antibodies that inhibit the binding of IgE to basophils and mast cells said peptide is about 25 and about 29 amino acids in length cyclized with two cysteine residues separated by about 23 amino acid residues, the sequence of said peptide corresponds to AA413 to A435 of the epsilon heavy chain of a mammalian IgE-CH3 and an analogue of the peptide wherein from one to four of the residues in AA413-AA435 are conservatively substituted, inserted, or deleted as recited in claim 29. The parent application does not have support for the claimed limitation "An IgE-CH3 domain antigen peptide" in claim 2. The parent application does not have support for the claimed limitation "one or more IgE-CH3 domain antigen peptide" in claims 19 and 20.

13. Claims 2, 19-20 and 29 are rejected under 35 U.S.C. 102(e) (2) as being anticipated by US Pat No. 6,228,987 B1 (May 2001, PTO 892).

The '987 patent teaches a peptide such as SEQ ID NO: 95 that is 25 amino acid in length, which is between about 25 and about 29 amino acids in length containing two cysteine residues separate by 23 amino acid residues (See entire document, SEQ ID NO: 95 of '987 patent). The reference peptide is 100% identical to the claimed peptide of SEQ ID NO: 5. The '987 patent further teach a peptide conjugate such as keyhole limpet hemocyanin (KLH), which is a carrier protein, covalently linked (conjugated) to the reference peptide (See column 16, line 34, in particular). Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 1/10/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) the present application enjoys an effective filing date of June 20, 1998. The parent application serial no. 09/100,287 was filed on the same day, June 20, 1998.

However, the parent application 09/100,287 does not have support for the claimed limitation of an IgE-CH3 domain antigen peptide useful for eliciting antibodies that inhibit the binding of IgE to basophils and mast cells said peptide is about 25 and about 29 amino acids in length cyclized with two cysteine residues separated by about 23 amino acid residues, the sequence of said peptide corresponds to AA413 to A435 of the epsilon heavy chain of a mammalian IgE-CH3 and an analogue of the peptide wherein from one to four of the residues in AA413-AA435 are conservatively substituted, inserted, or deleted as recited in claim 29. The parent application does not have support for the claimed limitation "An IgE-CH3 domain antigen peptide" in claim 2. The parent application does not have support for the claimed limitation "one or more IgE-CH3 domain antigen peptide" in claims 19 and 20.

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 2, 19-20 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable US Pat No. 6,025,468 A (Feb 2000, PTO 892) or US Pat No. 6,228,987 B1 (May 2001, PTO 892) each in view of WO 95/26365 publication and Nissim *et al* (J Immunology 150: 1365-74, Feb 1993; PTO 892).

The teachings of the '468 patent and the '987 patent have been discussed supra.

The claimed invention in claim 29 differs from the teachings of the references only that the IgE-CH3 domain antigen peptide corresponds to amino acid 413-435 of the epsilon heavy chain of a mammalian IgE-CH_3.

The WO 95/26365 publication teaches various mammalian IgE IgE-CH_3 domain such as human, rat and mouse (See Table 2 in pages 8-9, in particular). The WO 95/26365 publication further teaches that IgE domain peptide is useful for eliciting the production of antibodies to inhibit mast cell activation and to reduce allergen-induced IgE production (See abstract, in particular).

Nissim *et al* teach that IgE interaction with the low and high affinity Fc receptors on mast cells and basophils resides in the third constant domain of IgE (Cε) and that the amino acid residues determining the species specificity of the low affinity receptor such as FcεRII are no contained in the first 16 amino acids of the Cε3 domain (See abstract, in particular). Nissim *et al* further teach that in the mouse, Cε3 is the main domain involved in the binding to the murine low affinity receptor, and that the Cε4 domain influences this binding (See page 1366, column 1, first full paragraph, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the IgE CH3 domain antigen peptide as taught by the '468 patent or the '987 patent for the IgE CH3 domain from other mammal such as mouse and rat as taught by the WO 95/26365 publication having two terminal cysteine residues as taught by the

'468 patent or the '987 patent for an IgE-CH3 domain antigen peptide useful for eliciting antibodies that inhibit the binding of IgE to IgE receptors on basophils and mast cells. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Nissim *et al* teach that in the mouse, Cε3 is the main domain involved in the binding to the murine low affinity receptor, and that the Cε4 domain influences this binding (See page 1366, column 1, first full paragraph, in particular). The WO 95/26365 publication teaches that IgE domain peptide is useful for eliciting the production of higher titer antibodies to inhibit mast cell activation and reduce allergen-induced IgE production (See abstract, in particular). The term "about" expands the peptide to read on the reference IgE-CH3 domain as taught by the WO95/26365 publication.

17. SEQ ID NOS: 6-8 and 84 stand free of prior art.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any

inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

20. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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Patent Examiner
Technology Center 1600
August 25, 2003

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